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Drug Utilization Evaluation of Metronidazole at a Tertiary Care Center in Hyderabad, India

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ABSTRACT

Drug use evaluation is an on-going, systematic, criteria-based program of medicine evaluations that will help ensure appropriate medicine use. If therapy is determined to be inappropriate, interventions with providers or patients will be necessary to optimize pharmaceutical therapy. In our study we have developed a data collection form based upon WHO guidelines for conducting a DUE study on metronidazole use evaluation. To assess the usage of metronidazole at a tertiary care center Hyderabad a retrospective evaluation of usage patterns was carried out for the period of 6 months corresponding to the dates to 1-1-2018 to 30-6-2018. For conducting the evaluation process we had followed the standard guide lines formulated by WHO. The gender distribution of case sheets were male- 69, female- 80. Indication wise the distribution of case sheets were -43.23% are prophylaxis and surgical prophylaxis, 32.81% are non-indicated and 18, 96% were given for infections. The minimum number of days of treatment was 1 day and the maximum number of days of treatment was 23 days. All patient folders evaluated with regards to cellulitis, gynaecological surgeries, UTI, LRTI etc were found to meet the standard criteria appropriate for metronidazole use with respect to dose, and dose frequency. However, in the case of duration the evaluation was found to be largely inappropriate for all the justified indications. In addition, 34.81% of metronidazole use for unjustified indications was noted. This means that metronidazole has been deviated from standard treatment guidelines hence it facilitates the development of resistant strains to metronidazole and of no use in the near future, and it also affect the patient economically.

Keywords: DUE, Metronidazole, WHO, tertiary care center, Hyderabad.

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INTRODUCTION

Drug use evaluation is an ongoing, systematic, criteria-based program of medicine evaluations that will help ensure appropriate medicine use. If therapy is determined to be inappropriate, interventions with providers or patients will be necessary to optimize pharmaceutical therapy. A DUE can be structured so that it will assess the actual process of administering or dispensing a medicine (i.e., appropriate indications, dose, medicine interactions) or assess the outcomes. The following eight steps outline the basic information necessary to start and maintain a DUE Program.

Establish Responsibility: Responsibility falls to the DTC or a subcommittee of the DTC that functions only to monitor DUEs In the hospital or clinic. The DTC should undertake this responsibility with considerable interest, because this process can solve many medicine use problems, as has proven to be the Case in many countries where this quality assurance function has been fully utilized. The DTC or a subcommittee must establish procedures that will govern the committee in its activities concerning medicine use review and evaluation. As part of the responsibility of the DUE function, the DTC must establish a plan, outlining which medicines will be a part of the DUE process. This plan needs to be updated and evaluated each year.

Develop Scope of Activities

The DTC should assess and identify medicine use problems and using this information to develop a scope of activity for the DUE program. The scope can be extensive, or it can focus on a single aspect of pharmaceutical therapy. Methods to identify medicine use problems include and ABC or vital, essential, nonessential (VEN) analysis, defined daily dose analysis, ADR reports, medication error reports, antibiotic sensitivity results, procurement studies, hospital and primary care clinic indicator studies, patient complaints or

feedback, and staff feedback. These screening mechanisms serve to provide the DTC with information concerning medicine use that would need further evaluation in a DUE.

Establish Criteria, Define and Establish Thresholds

Criteria are statements that define correct medicine use. Establishing criteria is the single most important procedure in a DUE. Criteria for the use of any medicine should be established by the DTC using relevant evidence based literature sources and recognized international and local experts. The criteria for any DUE should reflect what is in the country's STGs (assuming that they have been developed correctly) and any medicine-use protocols that exist. Credibility of the DUE relies on criteria that are based on evidence-based medicine. Criteria must be developed with and accepted by the medical staff for the process to be credible. Criteria should be developed for three to five of the most important indicators for each aspect of medicine use. Reviewing larger numbers of indicators will make for a more difficult DUE process and may significantly impair the outcomes of the review. This is not to say that more extensive use of indicators should not be reviewed; only that results are more easily obtained and possibly more meaningful when the scope is narrowed to include only the most Important aspects of care. After developing criteria, the DTC must establish a threshold or standard (benchmark) against which the criteria will be judged. A threshold refers to the percentage of charts or records that will meet or exceed the established criteria for the medicine. Ideally, this threshold will be 100 percent, but realistically, a smaller percentage will be more appropriate to account for exceptions to routine medicine prescribing. Therefore, a threshold of 90 to 95 percent is typically used for many criteria, but each instance must be carefully analyzed before reaching a conclusion.

Collect Data and Organize Results.

DUEs can be accomplished as prospective evaluations, or they can be performed retrospectively. A prospective analysis involves the collection of data as the medicine is being prepared or dispensed to the patient. Retrospective analysis is done using chart reviews or other data sources to review medicine use according to indicators and criteria prepared in advance. The advantage of a prospective review is that the pharmacist (or other reviewer) can intervene at the time the medicine is dispensed to prevent errors in, for example, dosage, indications, or interactions. Retrospective evaluation, which may involve more of the reviewer's time or require access to medical records, is best accomplished when the reviewer has time away from the patient care areas and distractions.

Analyze Data

Data are collected, tabulated, and analyzed to see if criteria and thresholds are met. The following important steps should be completed when analyzing data—

• Tabulate results for each indicator

• Analyze results to see if the criteria are met and the thresholds are not exceeded

• Determine why thresholds are not met

• Analyze data quarterly or more frequently

If a threshold is not met, it may indicate a medicine use problem that requires the attention of the DTC.

Develop Recommendations and Action Plan

After completing the data analysis, information is presented to the DTC and a decision is made as to the appropriateness of the information in the DUE. The DTC also must decide on whether to continue, discontinue, or expand the functions of the DUE in question. All medicines that do not meet the thresholds must be evaluated carefully and plans must be made to improve the use of the medicine relative to the criteria.

Recommendations should be prepared for the DTC to address the following—

• Inappropriate medicine use

• Unacceptable patient outcomes

• Methods to resolve any medicine use problem

Recommendations should include specific steps to correct any medicine use problem that is evident from performing the DUE. For example, if a specific medicine is being prescribed at a high dose, then the recommendations need to reflect this and how the DTC might improve the dosing of this medicine. Interventions to improve medicine use might include—

• Education, including letters to practitioners, in-service education, workshops, newsletters, and faceto-face discussions

• Implementation of medicine order forms

• Prescribing restrictions

• Formulary manual changes

• Change (or better enforcement) of the STGs.

Conduct DUE Follow-up

Follow-up in every DUE is critical to ensure resolution of any unresolved medicine use problems. The DUE may have identified new problems that need to be resolved within the health care system. If the problems are not resolved, then the DUE will have little usefulness to the health care system. As a part of a follow-up plan, the DTC must assess the need to continue, modify, or stop the DUE activity depending on the results of each specific medicine review. A DUE should be an on-going process in which medicine related problems are regularly addressed. Medicine review should be considered a long-term program, one that is continuously updated and revised to reflect current situations and needs within the health care institution. All programs within the DTC should be evaluated yearly. This complete evaluation is necessary to look comprehensively at the entire program and analyze its merits and its utility in improving medicine use. Programs that do not have a significant impact on medicine use should be redesigned so that they can provide measurable improvements. Without improvements in medicine use and patient outcomes, the time spent on DUE will be of no value. It must be stressed that indicators and criteria for a DUE can be highly individualized depending on the specific needs of the health care facility.[1,2]

Metronidazole:

Metronidazole, a nitroimidazole, exerts antibacterial effects in an anaerobic environment against most obligate anaerobes. Once metronidazole enters the organism by passive diffusion and is activated in the cytoplasm of susceptible anaerobic bacteria, it is reduced; this process includes intra-cellular electron transport proteins such as ferredoxin, transfer of an electron to the nitro group of the metronidazole, and formation of a short-lived nitroso free

radical. Because of this alteration of the metronidazole molecule, a concentration gradient is created and maintained which promotes the drug's intracellular transport. The reduced form of metronidazole and free radicals can interact with DNA leading to inhibition of DNA synthesis and DNA degradation leading to death of bacteria. The precise mechanism of action of metronidazole is unclear.

Metronidazole Indications:

Metronidazole is indicated in the following conditions:

Treatment of Anaerobic Bacterial Infections Metronidazole Injection, USP is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria. Indicated surgical procedures should be performed in conjunction with Metronidazole Injection, USP therapy. In a mixed aerobic and anaerobic infection, antibiotics appropriate for the treatment of the aerobic infection should be used in addition to Metronidazole Injection, USP. Metronidazole Injection, USP is effective in Bacteroides fragilis infections resistant to clindamycin, chloramphenicol and penicillin.

Intra-Abdominal Infections, including peritonitis, intra-abdominal abscess and liver abscess, caused by Bacteroides species including the B. fragilis group (B. fragilis, B. distasonis, B. ovatus, B. thetaiotaomicron, B. vulgatus), Clostridium species, Eubacterium species, Peptococcus species and Peptostreptococcus species.

Skin and Skin Structure Infections caused by Bacteroides species including the B. fragilis group, Clostridium species, Peptococcus species, Peptostreptococcus species and Fusobacterium species. **Gynecologic Infections**, including endometritis, endomyometritis, tubo-ovarian abscess and postsurgical vaginal cuff infection, caused by Bacteroides species including the B. fragilis group, Clostridium species, Peptococcus species, Peptostreptococcus species and Fusobacterium species.

Bacterial Septicemia caused by Bacteroides species including the B. fragilis group and Clostridium species. Bone and Joint Infections, as adjunctive therapy, caused by Bacteroides species including the B. fragilis group.

Central Nervous System (CNS) Infections, including meningitis and brain abscess, caused by Bacteroides species including the B. fragilis group.

Lower Respiratory Tract Infections, including pneumonia, empyema and lung abscess, caused by Bacteroides species including the B. fragilis group. Endocarditis caused by Bacteroides species including the B. fragilis group.

Prophylaxis: The prophylactic administration of Metronidazole Injection, USP preoperatively, intraoperatively and postoperatively may reduce the incidence of postoperative infection in patients undergoing elective colorectal surgery which is classified as contaminated or potentially contaminated. Prophylactic use of Metronidazole Injection, USP should be discontinued within 12 hours after surgery. If there are signs of infection, specimens for cultures should be obtained for the identification of the causative organism(s) so that appropriate therapy may be given. To reduce the development of drug-resistant bacteria and maintain the effectiveness of Metronidazole Injection, USP and other antibacterial drugs, Metronidazole Injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Dose and Administration:

Dosage, rate of administration, and duration of treatment are to be individualized and depend upon the indication for use, the patient's age, weight, clinical condition and concomitant treatment, and on the patient's clinical and laboratory response to the treatment.

Loading Dose: 15 mg/kg infused intravenously over one hour (approximately 1 gram for a 70-kg adult).

Maintenance Dose: 7.5 mg/kg infused intravenously over one hour every six hours (approximately 500 mg for a 70-kg adult). The first maintenance dose should be instituted six hours following the initiation of the loading dose.[3]

Aim and objectives:

Aim: To assess the usage of metronidazole at a tertiary care hospital in Hyderabad compared to the indications for metronidazole use and standard treatment guidelines and provide recommendations to improve rational use of metronidazole at these hospitals and reduce the development of further antibiotic resistance, prevent ADRs associated with the drug, and to reduce the economic burden on the patient with inappropriate use.

Objectives:

- To analyse the pattern of metronidazole use among patient categories identified by age.
- To identify the illnesses most frequently treated with metronidazole
- To determine whether metronidazole was appropriately prescribed in respect of dose, dose frequency, and dose duration.
- To identify areas in which further information and education was needed by health care provider.
- To evaluate reason for stopping (discontinue)the drug is based on guide line or not.
- To assess whether the indication of metronidazole is on par with standard guidelines or not.
- To assess the frequency of ADRs associated with the drug use.
- To assess the potential and actual Drug-Drug interactions associated with metronidazole.

MATERIALS AND METHODS

Study Design: Retrospective Drug Utilization Evaluation Study.

Study Site: A tertiary Care Center at Hyderabad {Gandhi Hospital}, India.

Study Duration: 6 months.

Source of Data: A Data-collection form was developed based on WHO Guidelines.

Sample Size: 149.

Study Procedure: Since it is a retrospective study, we have collected all the case records from the medical record department from 1-01-2018 to 30-6-2018 that contained metronidazole in the prescription. A total of 149 case records

were obtained containing metronidazole as a drug in the prescription. During the process of evaluation, the prescriptions were analyzed for correct indication, correct dose, frequency, ADRs, Drug-Drug interactions, and contra-indications. The criteria established were adopted from standard treatment guidelines as formulated by FDA. The Threshold was developed by taking into consideration; the prescribing habits (KAP) of the doctors at these centers, the indicators are assigned with a threshold of 90-100%.

Study Design:

A retrospective evaluation of metronidazole usage patterns was carried out at a tertiary care hospital for the period of 6 months corresponding to the dates to 1-1-2018 to 31-6-2018.

For conducting the evaluation process we had followed the standard guide lines formulated by WHO.

Step 1 : Responsibility

The hospital where the study was conducted doesn't have DTCs and moreover the study is for academic purposes and hence the responsibility lied entirely with the students and guide.

Step 2. Scope of Activities

During the process of evaluation, the prescriptions were analyzed for correct indication, correct dose, frequency, ADRs, Drug-Drug interactions, and contra-indications.

Step 3.Criteria

Standard prescribing guidelines for metronidazole as formulated by FDA.

Step 4. Establishing Threshold

Taking into consideration, the prescribing habits (KAP) of the doctors at these centres, the indicators are assigned with a threshold of 90-100%.

Indicator	Criteria	Threshold%
Indication	PO, IV: Treatment of the following anaerobic infections: Intra-abdominal infections (may be used with a cephalosporin), Gynecologic infections, Skin and skin structure infections, Lower respiratory tract infections, Bone and joint infections, CNS infections, Septicemia, Endocarditis. IV Perioperative prophylactic agent in colorectal surgery. PO: Amebicide in the management of amebic dysentery, amebic liver abscess, and trichomoniasis: Treatment of peptic ulcer disease caused by Helicobacter pylori. Topical Treatment of acne rosacea. Vag:Management of bacterial vaginosis. Unlabeled Use: Treatment of giardiasis. Treatment of anti-infective associated pseudomembranous colitis.	**90%**
Dose and frequency and duration	PO (Adults): Anaerobic infections—7.5 mg/kg q 6 hr (not to exceed 4 g/day). Trichomoniasis—250 mg q 8 hr for 7 days orsingle 2-g dose or 1 g twice daily for 1 day. Amebiasis—500– 750 mg q 8 hr for 5– 10 days. H. pylori—250 mg 4 times daily or 500 mg twice daily for 1– 2 wk (with other agents). Bacterial vaginoses— 750 mg once daily as ER tablets for 7 days. Antibiotic associated pseudomembranous colitis—250– 500 mg 3– 4 times/day for 10– 14 days. PO (Infants and Children): Anaerobic infections—30 mg/kg/day divided q 6 hr, maximum dose: 4 g/day Trichomoniasis—15– 30 mg/kg/day divided q 8 hr for 7– 10 days. Amebiasis—35– 50 mg/kg/day divided q 8 hr for 5– 10 days (not to exceed 750 mg/dose). Antibiotic associated pseudomembranous colitis—30 mg/ kg/day divided q 6 hr for 7– 10 days. H. pylori—15– 20 mg/kg/day divided twice daily for 4 weeks. IV, PO (Neonates 0– 4 weeks, 1200 g): 7.5 mg/kg q 48 hr. Postnatal age 7 days, 1200– 2000 g—7.5 mg/kg/day q 24 hr. Postnatal age 7 days, 2000 g— 15 mg/kg/day divided q 12 hr. Postnatal age 7 days, 1200– 2000 g—15 mg/kg/ day divided q 12 hr. Postnatal age 7 days, 2000 g—30 mg/kg/day divided q 12 hr. IV (Adults): Anaerobic infections—Initial dose 15 mg/kg, then 7.5 mg/kg q 6– 8 hr or 500 mg q 6– 8 hr (not to exceed 4 g/day). Perioperative prophylaxis—Initial dose 15 mg/kg 1 hr before surgery, then 7.5 mg/kg 6 and 12 hr later. Amebiasis— 500– 750 mg q 8 hr for 5– 10 days. IV (Children): Anaerobic infections—30 mg/kg/day divided q 6 hr, maximum dose: 4 g/day. Topical (Adults): Acne rosacea—Apply thin film to affected area bid. Vag (Adults): Bacterial vaginosis—One applicatorful (5 g) 2 times daily for 5 days.	**95%**
contraindications	Contraindicated in: Hypersensitivity; Hypersensitivity to parabens (topical only); OB:First trimester of pregnancy. Use Cautiously in: History of blood dyscrasias; History of seizures or neurologic problems; Severe hepatic impairment (dosepsuggested); OB: Although safety not established, has been used to treat trichomoniasis in 2nd- and 3rd-trimester pregnancy— but not as single-dose regimen; Lactation: If needed, use single dose and interrupt nursing for 24 hr thereafter; Patients receiving corticosteroids or predisposed to edema (injection contains 28 mEq sodium/g metronidazole).	**100%**
Drug Interaction	Drug-Drug: Cimetidine may ↓ metabolism. Phenobarbital and rifampin may ↑ metabolism and may ↓ effectiveness. Metronidazole ↑ the effects of phenytoin, lithium, and warfarin. Disulfiram-like reaction may occur with alcohol ingestion. May cause acute psychosis and confusion with disulfiram ↑ risk of leukopenia with fluorouracil or azathioprine.	**90%**
Outcome	Negative culture/Improved symptomatology No treatment failure	**90%**

Step 5. Data collection and organisation.

The data was collected in data collection forms and organised according to the threshold percentage.

A total of 149 case sheets were obtained that contained metronidazole in the prescription between the period of 1-1-2018 to 30-6-2018.

Step 6.Data analysis.

The data obtained was analysed.

Step 7.Develop recommendations and Action plan.

Based on the results obtained, problematic areas were identified and appropriate recommendations were developed and shared with the concerned doctors and hospital authorities.

RESULTS AND DISCUSSION

This study provides the data on the use of metronidazole at a tertiary care Gandhi hospital. The considered parameters are age, gender, indication, dose, frequency, duration of therapy, contraindications and drug interacting with metronidazole.

Drug utilization pattern according to gender:

A total of 149 cases of metronidazole use were identified between the period from 1/1/18 - 30/6/18 patient. The distribution of cases on gender basis is 69 males (46.31%) and 80 females (53.69%).

Drug utilization pattern according to age:

The age range was between 4 months and 85 years. The usage pattern of metronidazole among various age groups are as follows: of 0-10 (2.013%), 11-20 (3.355%), 21-30yrs (17.449%) and 31-40 (24.832%), 41-50 (19.46%), 51-60 (24.16%), 61-70 (7.38%), 71-80 (0%), 81-90 (0.671%) and 91-100 (0%).

As per STGs, the percentage of metronidazole used (21%) was non indicated and it has'nt met the established criteria, and the rest used for infections (18.76%) , prophylaxis(28.75) and surgical prophylaxis(31.49) met the criteria.

Drug utilization pattern according to indication:

In our study, the percentage of metronidazole indicated in the conditions are :-

Infections:

urinary tract infections-2 (1.34%), cellulitis -4 (2.684%), pneumonitis -2 (1.34%), pseudocyst -4 (2.68%), liver abscess -5 (3.35%), schistomiasis -1 (0.67%), gastroenteritis -2 (1.34%), breast abscess -1 (0.67%), peritonitis -2 (1.34%), diarrhea -1 (0.67%), placenta infected -1 (0.67%), wound infection -1 (0.67%), acid peptic ulcer-1 (0.67%), infective endocarditis-1 (0.67%).

Diseases Not Indicated In Standard Guidelines:

fibroid uterus -7 (4.69%), postmenopausal bleeding -1 (0.67%), anemia -2 (1.34%), cystocele, rectocele,enterocele,hydrocele, meningocele -1 (0.67%), diabetic nephropathy -1 (0.67%), CKD – acute deterioration -6 (4.02%), AKI with CKD -6 (4.02%), uremic encephalopathy -6 (4.02%), bladder outlet obstruction -2 (1.34%), obstructive uropathy -2 (1.34%), retinopathy -4 (2.684%), febrile illness-2 (1.34%), thrombocytopenia-2 (1.34%), acute pancreatitis-3 (2.01%), chronic pancreatitis -7 (4.69%) , UTI bleed -2 (1.34%), oesophageal varies -3 (2.01%), ald -5 (3.35%), distal cbd -4 (2.684%), hepatic encephalopathy -2 (1.34%), ascites -4 (2.684%), portal hypertension-1 (0.67%), sigmoid diverticulitis -1 (0.67%), stomach ulcer -1 (0.67%), cld-1 (0.67%), supra condylar femur -1 (0.67%), pulmonary tb -1 (0.67%).

Prophylaxis:

septicemia -1 (0.67%), cva-2 (1.34%), status post adjunct chemotherapy -2 (1.34%), blood transfusion -4 (2.684%), sepsis -7 (4.69%), renal biopsy-1(0.67%), ijv catheter -7 (4.69%), hemodialysis -8 (5.3%), pd catheter -7 (4.69%), paraurethral tear after delivery -1 (0.67%), uteroplacental insufficiency -1 (0.67%), after delivery -2 (1.34%).

Post-Operative Prophylaxis

Laproscopic cystectomy -4 (2.684%), Myomectomy -4 (2.684%), Total abdominal hysterectomy -7 (4.69%), Lt bartollins cyst excision -2 (1.34%), Laparoscopic assisted vaginal hysterectomy (LAVH) -4 (2.684%), Pelvic floor repair -1 (0.67%), Dilation and curettage -2 (1.34%), Salpingoophorectomy -5 (3.35%), Infracolic oomentectomy -1 (0.67%), Salpingectomy -4(2.684%), ,Vaginoplasty -1(0.67%) , Tubal recanalisation -1 (0.67%), Laparoscopic surgery -1 (0.67%), Tubectomy -1 (0.67%), Laparatomy -1 (0.67%), Episiotomy –1 (0.67%),LSCS -1 (0.67%), Polypectomy -1 (0.67%), Laparoscopic ectopic resection -1 (0.67%), Marsupialization -1 (0.67%), Percutaneus nephrotomy -3 (2.01%), Appendectomy -1 (0.67%), Cystolithiomy -1 (0.67%), EVL-4 (2.684%)

Splenectomy -1(0.67%,ERCP+ biliary stent placement -1 (0.67%), Portosystemic shunt -1 (0.67%), Liver transplantation -1 (0.67%), Renal transplantation -1 (0.67%), Gastrectomy -1 (0.67%), Hemicolectomy -1 (0.67%), Papilotomy –ERCP -1 (0.67%), Cholecystectomy-1 (0.67%), Excision and repair meningocele -1 (0.67%).

Drug utilization pattern according to dose, ROA, Frequency, and the potential for interaction

In this research, the criteria of appropriateness of metronidazole use at the dose, dose frequency, dose duration were

The dose of metronidazole based on indication and duration given was 100ml/500 mg IV TID & 400mg oral TID .In all the indications studied, they met the benchmark requirement of 95%. Therefore metronidazole was used appropriately so far as dose was concerned.

Out of 149 cases, dose frequencies were eight hours and twenty four hours in 3cases(2.01%) and 146 cases(97.98%) respectively.

Dose, durations were mostly inappropriate for all the justified indications studied.

i.metronidazole is given more than thershold limit	36
ii.metronidazole is given according to thershold limit	34
iii.metronidazole is given less than thershold limit	79

Drug Interactions:

Metronidazole has interacted with a variety of concomitantly administered drugs-

Clarithryomycin	**0.67%**
Ondansetron	**10.70%**
Tramadol	**27.50%**
Ciprofloxacin	**11.40%**
Efavirenz	**0.67%**
Ofloxacin	**26.80%**
Atorvastatin	**2.01%**
Terlipressin	**2.01%**
Hydroxyzine	**1.34%**
Secnidazole	**0.67%**
without interactions	**26.18%**

Culture and Sensitivity Test:

As per standard guidelines culture test is necessary to promote rationalize drug therapy. In gastroenterology department out of 41 cases only (7.31%) 3 cases have done with the test. In gynecological department no test has been performed. In nephrology department out of 36 cases only (2.71%) 1 case done with the test. In general medicine no test has been performed.

Reason for Ceasing Metronidazole:

Discharge with other class of antibiotic (12.08%), course completed (48.99%), change to narrow agent (20.13%), organism resistant(10.73%), patient expired(4.02%), patient discharge with metronidazole(1.34%), culture –ve(2.68%).

Drug utilization pattern according to contraindications:

As per STGs, metronidazole is contraindicated in first trimester of pregnancy. In our study, out of 149 cases, 149cases are met threshold according to STG's.

Outcomes:

34.84% of the cases received metronidazole for non-indications, 24% of the cases are without interactions, 22.81% met the threshold for duration of therapy, 10.02% cases have undergone culture sensitivity test.

Metronidazole is a broad spectrum antibiotic belongs to class nitroimidazoles. Now a days metronidazole is irrationally prescribed globally particularly in India. Hence it facilitates the development of resistant strains to metronidazole. And is more prone to cause complications (ADR's) like asceptic meningitis, encephalopathy, seizures and common symptoms like headache, dizziness, abdominal pain, anorexia it is not usually indicated in pregnancy except in life threatening conditions**.**

Threats of resistance development to metronidazole

The development of resistance by microorganisms is of global concern. This is because microorganisms that were susceptible to some anti-infective agents have now become resistant. Unfortunately, irrational prescribing is a global problem. Studies on medicine prescribing in India have concluded that much of it is irrational. Making a prescribing decision is vital in the prevention of morbidity and mortality. The physician's prescribing decision is the result of input from patients, commercial sources, professional colleagues, academic literature, and government regulations. Ineffective use of these sources of information can result in a wide variety of prescribing errors. Medicine utilization review is the most common and structured approach used to examine patterns of medicine use and to determine levels of appropriateness in prescribing. Medicine usage reviews are essential in order to establish the extent of rational and irrational prescribing and to deliver better healthcare services. Antimicrobials, like any other medicines, may be used inappropriately.

A prescriber may choose an inappropriate type of antimicrobial, taking into account the clinical condition, resistance patterns and cost. Continuing antimicrobial misuse leads not only to poor patient outcome, unnecessary adverse reactions and wasted resources, but also to emerging resistance of bacteria to antimicrobials. Antimicrobials can also be very expensive, and in most facilities they constitute a major portion of the drug budget. The phenomenon of resistance is seen not only in bacteria and mycobacteria (multidrug resistant TB, for example), but also in protozoal infections (resistance to chloroquine as an antimalarial) and viral infections (HIV and antiretrovirals).

CONCLUSION

All patient folders evaluated with regards to cellulitis,gynecological surgeries ,uti,lrti etc were found to meet the standard criteria appropriate for metronidazole use with respect to dose, and dose frequency.

However, in the case of duration the evaluation was found to be largely inappropriate for all the justified indications. In addition, 34.81% of metronidazole use for unjustified indications was noted. This means that metronidazole has been deviated from standard treatment guidelines hence it facilitates the development of resistant strains to metronidazole and of no use in the near future, and it also effect the patient economically.

RECOMMENDATION

Health care providers must be periodically updated with the national standard treatment guidelines. It is further recommended that the hospital's management attention be drawn to the draw backs observed regarding the inappropriate use and duration of metronidazole, so that specific interventions could be initiated to improve its use for excellent outcomes. Following the implementation of the interventions, another DUE should be conducted to determine the level of adherence to the acceptable standards and its impact on patient outcomes.

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ABBREVIATIONS USED

ABC -always better control

ADR - adverse drug reaction

ATC -anatomic therapeutic chemical codes

CCU -critical care unit

CDC -center for disease control

DDD -defined daily dosage

DTC-drug and therapeutic commitee

DUR - drug utilization review

DUE -drug utilization evaluation

HCP -health care professionals

INRUD -international network for rational use of drugs

ME - medication errors

MUE - medication use evaluation

PPMS-prescription pattern monitoring studies

RUM -rational use of medicines

STG's-standard treatment guidelines

VEN -vital essential nonessential

WHO -world health organization

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